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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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LEYDIG VOIT & MAYER, LTD
TWO PRUDENTIAL PLAZA, SUITE 4900
180 NORTH STETSON AVENUE
CHICAGO, IL 60601-6780

EXAMINER
DAVIS, RUTH A

ART UNIT	PAPER NUMBER
1651	3

DATE MAILED: 02/11/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/046,517	KOVESDI ET AL.	
	Examin r	Art Unit	
	Ruth A. Davis	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for R ply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-26* is/are pending in the application.

4a) Of the above claim(s) *15-26* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-26* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *2* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

1. Restriction to one of the following inventions is required under 35 U.S.C. 121:

   I. Claims 1 – 14, drawn to a composition, classified in class 424, subclass 600, for example.

   II. Claims 15 – 18, drawn to a method for preserving a viral vector, classified in class 435, subclass 440, for example.

   III. Claims 19 – 26, drawn to a method for administering a viral vector, classified in class 424, subclass 204.1, for example.

The inventions are distinct, each from the other because of the following reasons:

2. Inventions I:II and I:III are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case other materially different products could be used to preserve viral vectors such as block copolymers of alpha-hydro-omega-hydroxypoly(oxyethylene)-poly(oxypropylene)-poly(oxyethylene). In addition, other materially different products could be used in the method for administering a viral vector such as a hydrogel matrix.

The inventions of groups II:III are directed to different inventions which are not connected in design, operation, and/or effect. These methods are independent since they are not

disclosed as capable of use together, they have different modes of operation, they have different functions, and/or they have different effects. One would not have to practice the various methods at the same time to practice just one method alone.

The several inventions above are independent and distinct, each from the other. They have acquired a separate status in the art as a separate subject for inventive effect and require independent searches (as indicated by the different classification). The search for each of the above inventions is not co-extensive particularly with regard to the literature search. Further, a reference which would anticipate the invention of one group would not necessarily anticipate or even make obvious another group.

Because these inventions are distinct for the reasons given above and the search required for one group is not required for the other groups, restriction for examination purposes as indicated is proper.

3. During a telephone conversation with John Kilyk on January 28, 2003 a provisional election was made with traverse to prosecute the invention of Group I, claims 1 - 14. Affirmation of this election must be made by applicant in replying to this Office action. Claims 15 – 26 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

4. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the

application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Claim Rejections - 35 USC § 112

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 5 and 6 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 5, line 1, "the nonionic surfactant" lacks sufficient antecedent basis.

In claim 6, line 2, "FFU/ml" is rendered indefinite because it is unclear if applicant intends the phrase to read "PFU/ml".

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this

subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

8. Claims 1 - 7, 9, 11 and 13 are rejected under 35 U.S.C. 102(a) as being anticipated by Evans et al. (WO 01-66137).

Applicant claims a composition for maintaining a non-enveloped viral vector, the composition comprising about 1 – 25% trehalose; about 0.02 – 2 mM divalent metal salt, cationic polymer or combination thereof; a multiplicity of non-enveloped viral vector particles; and a liquid carrier. Specifically the composition comprises about 0.05 – 2 mM divalent metal salt, or 0.05 – 2 mM MgCl2. The composition further comprises a nonionic surfactant in about 0.001 – 0.015%, wherein the nonionic surfactant is polysorbate 80 and also comprises a buffer, such that the pH is about 6 – 9 at 25C. The concentration of non-enveloped viral vectors are about 1X10^5 – 1X10^13 PFU/ml, the osmolality of the liquid composition is about 150 – 800 mOsM and the viral vector is an adenoviral vector.

Evans teaches viral compositions comprising a liquid adenovirus, buffer, sugar, salt, divalent cation and non-ionic detergent (abstract). The compositions are disclosed to maintain viral stability for up to 2 years at temperatures of 2 – 8C and higher (p.1,3). Specifically, the composition comprises an adenovirus in an amount of 1x10^7 virus particles/milliliter – 1x10^13 particles/milliliter (p.8). Non-ionic surfactants include polysorbate 80 (p.9) at about 0.001 – 1% (p.11), divalent cations include MgCl2 at about 0.1 – 5 mM (p.9), and the sugar may be trehalose (p.9). Evans teaches the salts are added to attain the desired ionic strength and osmolarity (0054) with preferred osmolarties between 200 – 800 mOs/L (p.10) and a preferred pH of 7 – 9 (p.8).

The reference anticipates the claimed subject matter.

9. Claims 1 – 7, 9, 11 and 13 are rejected under 35 U.S.C. 102(e) as being anticipated by Evans et al. (US 2002/0041881 A1).

Applicant claims a composition for maintaining a non-enveloped viral vector, the composition comprising about 1 – 25% trehalose; about 0.02 – 2 mM divalent metal salt, cationic polymer or combination thereof; a multiplicity of non-enveloped viral vector particles; and a liquid carrier. Specifically the composition comprises about 0.05 – 2 mM divalent metal salt, or 0.05 – 2 mM MgCl2. The composition further comprises a nonionic surfactant in about 0.001 – 0.015%, wherein the nonionic surfactant is polysorbate 80 and also comprises a buffer, such that the pH is about 6 – 9 at 25C. The concentration of non-enveloped viral vectors are about 1X10^5 – 1X10^13 PFU/ml, the osmolality of the liquid composition is about 150 – 800 mOsM and the viral vector is an adenoviral vector.

Evans teaches viral compositions comprising a liquid adenovirus, buffer, sugar, salt, divalent cation and non-ionic detergent (abstract). The compositions are disclosed to maintain viral stability for up to 2 years at temperatures of 2 – 8C and higher (0004, 0012). Specifically, the composition comprises an adenovirus in an amount of 1x10^7 virus particles/milliliter – 1x10^13 particles/milliliter (0050). Non-ionic surfactants include polysorbate 80 (0051) at about 0.001 – 1% (0059), divalent cations include MgCl2 at about 0.1 – 5 mM (0052), and the 2 – 8% sugar/cryoprotectant may be trehalose (0053, 0060, 0061). Evans teaches the salts are added to attain the desired ionic strength and osmolarity (0054) with preferred osmolarties between 200 – 800 mOs/L (0056) and a preferred pH of 7.5 – 8.5 (0059).

The reference anticipates the claimed subject matter.

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

12. Claims 1 and 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kuma et al. (EP 0872249 A1).

Applicant claims a composition for maintaining a non-enveloped viral vector, the composition comprising about 1 – 25% trehalose; about 0.02 – 2 mM divalent metal salt, cationic polymer or combination thereof; a multiplicity of non-enveloped viral vector particles; and a liquid carrier, wherein the viral vector is an adenovirus.

Kuma teaches preserving viruses by adding 1 – 10% arginine, 1 – 10% trehalose, polyethylene glycol (cationic polymer) and buffer to an adenovirus (col.5 line 41 – col.6 line 28).

Kuma does not teach the claimed amounts of cationic polymer. However, at the time of the claimed invention, it would have been well within the purview of one of ordinary skill in the art to optimize the amounts of known effective ingredients as a matter of routine experimentation. Therefore, at the time of the claimed invention, one of ordinary skill in the art would have been motivated by routine practice to optimize the volumes of each of the ingredients of Kuma with a reasonable expectation for successfully obtaining a composition for preserving viruses.

13. Claims 1 – 3 and 6 – 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Herrmann et al. (US 5792643).

Applicant claims a composition for maintaining a non-enveloped viral vector, the composition comprising about 1 – 25% trehalose; about 0.02 – 2 mM divalent metal salt, cationic polymer or combination thereof; a multiplicity of non-enveloped viral vector particles; and a liquid carrier. Specifically the composition comprises about 0.05 – 2 mM divalent metal salt, or 0.05 – 2 mM MgCl2. The composition further comprises a buffer, such that the pH is about 6 – 9 at 25C and 10 – 65 mM arginine. The concentration of non-enveloped viral vectors are about 1X10^5 – 1X10^13 PFU/ml, the osmolality of the liquid composition is about 150 – 800 mOsM, the ionic strength of the liquid composition is about 10 – 200 mM.

Herrmann teaches stabilizing viral particles by adding thereto a saccharide, buffer and water (abstract). Specifically, compositions of buffer, 1 – 12% trehalose, 0.03% or less NaCl and 0.1 – 10% arginine are combined with a retrovirus to obtain an aqueous solution with a pH

of about 7.4 (col.3, example 3). Other salts may also be added such as magnesium chloride (col.7 line 1-5).

Herrmann does not specifically teach the claimed amounts of each ingredient, the claimed osmolality or ionic strength. However, at the time of the claimed invention, it would have been well within the purview of one of ordinary skill in the art to optimize the amounts of known effective ingredients as well as osmolalities and ionic strengths as a matter of routine experimentation. Therefore, at the time of the claimed invention, one of ordinary skill in the art would have been motivated by routine practice to optimize the parameters of the composition of Herrmann with a reasonable expectation for successfully obtaining a composition for stabilizing viruses.

14. Claims 1 – 9 and 11 – 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Evans et al. (US 2002/0041881 A1) or Evans et al. (WO 01/66137).

Applicant claims a composition for maintaining a non-enveloped viral vector, the composition comprising about 1 – 25% trehalose; about 0.02 – 2 mM divalent metal salt, cationic polymer or combination thereof; a multiplicity of non-enveloped viral vector particles; and a liquid carrier. Specifically, the composition comprises about 0.05 – 2 mM divalent metal salt, or 0.05 – 2 mM MgCl2. The composition further comprises a nonionic surfactant in about 0.001 – 0.015%, wherein the nonionic surfactant is polysorbate 80; and a buffer, such that the pH is about 6 – 9 at 25C. The concentration of non-enveloped viral vectors are about 1X10^5 – 1X10^13 PFU/ml, the osmolality of the liquid composition is about 150 – 800 mOsM and the

ionic strength of the liquid composition is about 10 – 200 mM. The viral vector is an adenoviral vector and is replication deficient.

Evans (US) teaches viral compositions comprising a liquid adenovirus, buffer, sugar, salt, divalent cation and non-ionic detergent (abstract). The compositions are disclosed to maintain viral stability for up to 2 years at temperatures of 2 – 8C and higher (0004, 0012). Specifically, the composition comprises an adenovirus in an amount of 1x10^7 virus particles/milliliter – 1x10^13 particles/milliliter (0050). Non-ionic surfactants include polysorbate 80 (0051) at about 0.001 – 1% (0059), divalent cations include MgCl2 at about 0.1 – 5 mM (0052), and the 2 – 8% sugar/cryoprotectant may be trehalose (0053, 0060, 0061). Evans (US) teaches the salts are added to attain the desired ionic strength and osmolarity (0054) with preferred osmolarties between 200 – 800 mOs/L (0056) and a preferred pH of 7.5 – 8.5 (0059).

Evans (WO) teaches viral compositions comprising a liquid adenovirus, buffer, sugar, salt, divalent cation and non-ionic detergent (abstract). The compositions are disclosed to maintain viral stability for up to 2 years at temperatures of 2 – 8C and higher (p.1,3). Specifically, the composition comprises an adenovirus in an amount of 1x10^7 virus particles/milliliter – 1x10^13 particles/milliliter (p.8). Non-ionic surfactants include polysorbate 80 (p.9) at about 0.001 – 1% (p.11), divalent cations include MgCl2 at about 0.1 – 5 mM (p.9), and the sugar may be trehalose (p.9). Evans (WO) teaches the salts are added to attain the desired ionic strength and osmolarity (0054) with preferred osmolarties between 200 – 800 mOs/L (p.10) and a preferred pH of 7 – 9 (p.8).

The references do not teach the compositions with the claimed ionic strength, or wherein the virus is replication deficient. However, at the time of the claimed invention, it would have

been well within the purview of one of ordinary skill in the art to optimize the parameters of the compositions of Evans (US) and/or Evans (WO) as a matter of routine experimentation. Moreover, at the time of the claimed invention, one of ordinary skill in the art would have been motivated by routine practice to optimize the parameters of the above compositions with a reasonable expectation for successfully obtaining a composition for maintaining a viral vector.

15. Claims 1 – 2 and 4 – 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kovesdi (WO 00/34444).

Applicant claims a composition for maintaining a non-enveloped viral vector, the composition comprising about 1 – 25% trehalose; about 0.02 – 2 mM divalent metal salt, cationic polymer or combination thereof; a multiplicity of non-enveloped viral vector particles; and a liquid carrier. Specifically, the composition comprises about 0.05 – 2 mM divalent metal salt. The composition further comprises a nonionic surfactant in about 0.001 – 0.015%, wherein the nonionic surfactant is polysorbate 80; a buffer, such that the pH is about 6 – 9 at 25C; and about 10 – 65 mM arginine. The concentration of non-enveloped viral vectors are about 1X10^5 – 1X10^13 PFU/ml, the osmolality of the liquid composition is about 150 – 800 mOsM and ionic strength of the liquid composition is about 10 – 200 mM. Finally, the viral vector is a replication deficient adenoviral vector.

Kovesdi teaches a composition for preserving a virus, the composition comprising a liquid carrier, viral particles, polysorbate 80, L-arginine and trehalose (abstract). The composition additionally comprises adenovirus (p.2 line 31-34, p.3 line 11-19), tris buffer, and salts (p.3 line 26-30). The trehalose is present at about 2 – 10%, the polysorbate is present at

about 0.001 – 0.01% (p.4 line4-12) while the temperature is from 2 – 37C (p.5 line 27-34), and the pH is from 6 – 9 (p.6 line 32-37). Kovesdi teaches the compositions comprising divalent metal salts to include NaCl (examples).

Kovesdi does not teach the composition with the claimed amounts of each ingredient, ionic strength, osmolality, or wherein the virus is replication deficient. However, at the time of the claimed invention, it would have been well within the purview of one of ordinary skill in the art to optimize the amounts of known effective ingredients as well as the parameters of the compositions of Kovesdi as a matter of routine experimentation. Moreover, at the time of the claimed invention, one of ordinary skill in the art would have been motivated by routine practice to optimize the parameters of the disclosed composition with a reasonable expectation for successfully obtaining a composition for preserving a virus.

16. Claims 1 – 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Evans (US) or Evans (WO), in view of Kovesdi (WO).

Applicant claims a composition for maintaining a non-enveloped viral vector, the composition comprising about 1 – 25% trehalose; about 0.02 – 2 mM divalent metal salt, cationic polymer or combination thereof; a multiplicity of non-enveloped viral vector particles; and a liquid carrier. Specifically the composition comprises about 0.05 – 2 mM divalent metal salt, or 0.05 – 2 mM MgCl2. The composition further comprises a nonionic surfactant in about 0.001 – 0.015%, wherein the nonionic surfactant is polysorbate 80; a buffer, such that the pH is about 6 – 9 at 25C; and about 10 – 65 mM arginine. The concentration of non-enveloped viral vectors are about 1X10^5 – 1X10^13 PFU/ml, the osmolality of the liquid composition is about

150 – 800 mOsM, the ionic strength of the liquid composition is about 10 – 200 mM. Finally, the viral vector is a replication deficient adenoviral vector.

Evans (US) teaches viral compositions comprising a liquid adenovirus, buffer, sugar, salt, divalent cation and non-ionic detergent (abstract). The compositions are disclosed to maintain viral stability for up to 2 years at temperatures of 2 – 8C and higher (0004, 0012). Specifically, the composition comprises an adenovirus in an amount of 1x10^7 virus particles/milliliter – 1x10^13 particles/milliliter (0050). Non-ionic surfactants include polysorbate 80 (0051) at about 0.001 – 1% (0059), divalent cations include MgCl2 at about 0.1 – 5 mM (0052), and the 2 – 8% sugar/cryoprotectant may be trehalose (0053, 0060, 0061). Evans (US) teaches the salts are added to attain the desired ionic strength and osmolarity (0054) with preferred osmolarties between 200 – 800 mOs/L (0056) and a preferred pH of 7.5 – 8.5 (0059).

Evans (WO) teaches viral compositions comprising a liquid adenovirus, buffer, sugar, salt, divalent cation and non-ionic detergent (abstract). The compositions are disclosed to maintain viral stability for up to 2 years at temperatures of 2 – 8C and higher (p.1,3). Specifically, the composition comprises an adenovirus in an amount of 1x10^7 virus particles/milliliter – 1x10^13 particles/milliliter (p.8). Non-ionic surfactants include polysorbate 80 (p.9) at about 0.001 – 1% (p.11), divalent cations include MgCl2 at about 0.1 – 5 mM (p.9), and the sugar may be trehalose (p.9). Evans (WO) teaches the salts are added to attain the desired ionic strength and osmolarity (0054) with preferred osmolarties between 200 – 800 mOs/L (p.10) and a preferred pH of 7 – 9 (p.8).

The references do not teach the compositions further comprising arginine. However, Kovesdi teaches a composition for preserving a virus, the composition comprising a liquid

carrier, adenoviral particles, polysorbate 80, L-arginine and trehalose (abstract, p.2 line 31-34, p.3 line 11-19). At the time of the claimed invention, one of ordinary skill in the art would have been motivated to include arginine in the compositions of Evans (US) or Evans (WO) because of the known and disclosed use to preserve viruses. Moreover, at the time of the claimed invention, one or ordinary skill in the art would have been motivated to combine arginine to the composition of Evans (US) and/or Evans (WO) with a reasonable expectation for successfully obtaining a composition for preserving and maintaining viral compositions.

The references do not teach the compositions with the claimed ionic strength, or wherein the virus is replication deficient. However, at the time of the claimed invention, it would have been well within the purview of one of ordinary skill in the art to optimize the parameters of the compositions of Evans (US) and/or Evans (WO) as a matter of routine experimentation. Moreover, at the time of the claimed invention, one of ordinary skill in the art would have been motivated by routine practice to optimize the parameters of the above compositions with a reasonable expectation for successfully obtaining a composition for maintaining a viral vector.

17. Claims 1 – 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kovesdi in view of Frei et al. (WO 99/41416).

Applicant claims a composition for maintaining a non-enveloped viral vector, the composition comprising about 1 – 25% trehalose; about 0.02 – 2 mM divalent metal salt, cationic polymer or combination thereof; a multiplicity of non-enveloped viral vector particles; and a liquid carrier. Specifically the composition comprises about 0.05 – 2 mM divalent metal salt, or 0.05 – 2 mM MgCl2. The composition further comprises a nonionic surfactant in about

0.001 – 0.015%, wherein the nonionic surfactant is polysorbate 80; a buffer, such that the pH is about 6 – 9 at 25C; and about 10 – 65 mM arginine. The concentration of non-enveloped viral vectors are about 1X10^5 – 1X10^13 PFU/ml, the osmolality of the liquid composition is about 150 – 800 mOsM, the ionic strength of the liquid composition is about 10 – 200 mM. Finally, the viral vector is a replication deficient adenoviral vector.

Kovesdi teaches a composition for preserving a virus, the composition comprising a liquid carrier, viral particles, polysorbate 80, L-arginine and trehalose (abstract). The composition additionally comprises adenovirus (p.2 line 31-34, p.3 line 11-19), tris buffer, and salts (p.3 line 26-30). The trehalose is present at about 2 – 10%, the polysorbate is present at about 0.001 – 0.01% (p.4 line4-12) while the temperature is from 2 – 37C (p.5 line 27-34), and the pH is from 6 – 9 (p.6 line 32-37). Kovesdi teaches the compositions comprising divalent metal salts to include NaCl (examples).

Kovesdi does not teach the composition with the claimed amounts of each ingredient, ionic strength, osmolality, or wherein the virus is replication deficient. However, at the time of the claimed invention, it would have been well within the purview of one of ordinary skill in the art to optimize the amounts of known effective ingredients as well as the parameters of the compositions of Kovesdi as a matter of routine experimentation. Moreover, at the time of the claimed invention, one of ordinary skill in the art would have been motivated by routine practice to optimize the parameters of the disclosed composition with a reasonable expectation for successfully obtaining a composition for preserving a virus.

Kovesdi does not teach the composition wherein the salt is magnesium chloride. However, Frei teaches compositions comprising adenoviral particles buffered to maintain a pH

of 7 – 8.5 in the temperatures of 2 – 27C (abstract,p.8) wherein the compositions comprise about 5 – 25 mg/mL disaccharides, about 1x10^9 – 1X10^13 viral particles/mL (p.7), about 0.1 – 1 mg/mL divalent metal salts (magnesium salts) (p.5), diluents and about 0.01 – 0.3 mg/mL polysorbate 80 (p.7).

At the time of the claimed invention, one of ordinary skill in the art would have been motivated to use magnesium chloride as the salt of Kovesdi because of the known and disclosed use to preserve viruses. Moreover, at the time of the claimed invention, one or ordinary skill in the art would have been motivated to include MgCl2 in the composition Kovesdi with a reasonable expectation for successfully obtaining a composition for preserving and maintaining viral compositions.

Double Patenting

18. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

19. Claims 1 – 14 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 12 – 24 of U.S. Patent No. 6514943 or claims 13 – 20 of U.S. Patent No. 6225289, in view of Evans (US) or Evans (WO).

US Patent 6514943 claims a composition comprising an adenovirus, liquid carrier, and stabilizing agents selected from polysorbate 80, L-arginine, trehalose, or combinations thereof. The composition has 2 – 10% trehalose.

US 6225289 claims a liquid composition comprising adenoviral vector, liquid carrier, and a stabilizing agent selected from polysorbate 80, L-arginine, trehalose and combinations thereof. Specifically, 2 – 10% trehalose, 0.001 – 0.1% polysorbate 80, a buffer and salt.

Although the claims do not teach the composition comprising MgCl2, Evans (US) and Evans (W) teach viral compositions comprising a liquid adenovirus, buffer, sugar, salt, divalent cation and non-ionic detergent. The compositions are disclosed to maintain viral stability for up to 2 years at temperatures of 2 – 8C and higher. Specifically, the composition comprises an adenovirus in an amount of 1x10^7 virus particles/milliliter – 1x10^13 particles/milliliter. Non-ionic surfactants include polysorbate 80 at about 0.001 – 1%, divalent cations include MgCl2 at about 0.1 – 5 mM, and the 2 – 8% sugar/cryoprotectant may be trehalose. Evans teaches the salts are added to attain the desired ionic strength and osmolarity with preferred osmolarties between 200 – 800 mOs/L and a preferred pH of 7.5 – 8.5. Evans teaches that the MgCl2 is necessary for optimum adenovirus stability (example 5).

At the time of the claimed invention, one of ordinary skill in the art would have been motivated to use magnesium chloride as the salt of Kovesdi because of the known and disclosed use to stabilize, maintain and preserve viruses. Moreover, at the time of the claimed invention,

one or ordinary skill in the art would have been motivated to include MgCl2 in the composition Kovesdi with a reasonable expectation for successfully obtaining a composition for preserving and maintaining viral compositions.

In addition, at the time of the claimed invention, it would have been well within the purview of one of ordinary skill in the art to optimize the amounts of known effective ingredients as well as the parameters (ionic strength, osmolalities) of the compositions of Kovesdi as a matter of routine experimentation.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ruth A. Davis whose telephone number is 703-308-6310. The examiner can normally be reached on M-H (7:00-4:30); altn. F (7:00-3:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 703-308-0196. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Ruth A. Davis; rad
February 4, 2003

LEON B. LANKFORD, JR.
PRIMARY EXAMINER